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Transgender Health Concerns

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1 Introduction

1.1 Overview of Transgender Health Concerns

Transgender persons are those who live full-time or part-time in the gender role of the opposite biologic sex (Lawrence et al., 1996). Transgender persons share the same health concerns as nontransgender persons; as members of a minority group characterized by complex identities and often by visibly gender-variant social presentations, transgender persons also have special health concerns related to the delivery of health services in a manner that recognizes and takes account of their identities and presentations (see Chapter 26).

Transgender persons also have a number of other, more specific health concerns that are the focus of this chapter. Many transgender persons receive cross-sex hormone therapy, which must be managed carefully to maximize the beneficial effects and minimize complications and side effects. Some transgender persons undergo surgical procedures to masculinize or feminize their bodies, especially their genitals and breasts; these procedures can result in complications as well as benefits. Transgender persons who have undergone cross-sex hormone treatment may require screening for neoplasia in organ systems associated with both their birth sex and the sex with which they identify or to which they have been reassigned. Some male-to-female (MtF) transgender persons attempt to modify their bodies using injections of liquid silicone, which can be a source of significant morbidity and mortality. Some transgender persons have a high prevalence of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) and other sexually transmitted infections (STIs). Transgender persons appear to have an elevated prevalence of coexisting mental health problems. A disproportionate number of transgender persons attempt or complete suicide, engage in other forms of self-harm, and are victims of violence.

1.2 Health Concerns in Relation to Transgender Diversity

Transgender is an umbrella term that includes many diverse groups whose health concerns may differ substantially. Only a few categories

of transgender persons have been studied with reference to health concerns; these categories are not mutually exclusive and sometimes overlap significantly. *Transsexuals* comprise the most-studied transgender group; they are individuals who express extreme discomfort with their biologic sex, a phenomenon called *gender dysphoria*, and who typically seek hormone therapy and genital surgery to change their bodies to resemble the opposite sex (American Psychiatric Association [APA], 1987). Transsexualism is rare, affecting about 1 in 12,000 males and 1 in 30,000 females in Western countries (Bakker et al., 1993).

Another transgender group that has undergone significant study is MtF transgender sex workers, many of whom use cross-sex hormones; the size of the MtF transgender sex-worker population is unknown. Some MtF transgender sex workers are transsexuals; others are *transgenderists*, persons who usually live full-time in the cross-gender role and may use cross-gender hormones but who have not undergone, or do not wish to undergo, feminizing genital surgery (Docter & Prince, 1997).

Cross-dressers, or transvestites—men who dress in the clothing of the opposite sex for sexual excitement, gender expression, or both—probably comprise the largest transgender group. In one recent survey, 2.8% of adult males reported having experienced sexual arousal in association with cross-dressing (Langstrom & Zucker, 2005). The health concerns of cross-dressers have received little study, although it is recognized that some cross-dressers use cross-sex hormones to feminize their bodies (Docter & Fleming, 1992; Docter & Prince, 1997). Cross-dressers and MtF transsexuals share many characteristics in common (Docter & Fleming, 2001), suggesting that they comprise part of a continuum of MtF transgender expression, rather than representing discrete entities. With the exception of female-to-male (FtM) transsexuals, the spectrum of female transgender expression and the health concerns of female transgender persons have received little attention.

It should be apparent that the health concerns of an 18-year-old MtF transgender sex worker who takes nonprescribed cross-sex hormones and lives full-time in cross-gender role may be quite different from those of a 50-year-old male computer systems analyst who cross-dresses occasionally but does not take cross-sex hormones, even though both can be considered transgender persons. Consequently, when examining research findings relevant to transgender health concerns, it is important to consider the specific transgender populations in which studies were conducted to avoid unwarranted generalizations.

2 Cross-Sex Hormone Therapy in Transgender Persons

2.1 Overview and Criteria for Provision of Cross-Sex Hormone Therapy

Some transgender persons undergo cross-sex hormone treatment to look and feel more like members of the sex as which they present themselves or with which they identify. Cross-sex hormone therapy stimulates the development of secondary sex characteristics of the sex with which the person identifies and suppresses the secondary sex charac-

teristics of the person's birth sex. Several comprehensive reviews address the management of cross-sex hormone therapy in transgender persons (Meyer et al., 1986; Asscheman & Gooren, 1992; Schlatterer et al., 1996; Futterweit, 1998; Gooren, 1999, 2005; Oriel, 2000; Michel et al., 2001; Moore et al., 2003; Tangpricha et al., 2003; Dahl et al., 2006). Eligibility criteria and general guidelines for the conduct of cross-sex hormone therapy are also discussed in the *Standards of Care for Gender Identity Disorders* (*Standards of Care*) (Meyer et al., 2001), promulgated by the Harry Benjamin International Gender Dysphoria Association (HBIGDA), a professional group of transgender care specialists.

Hormone therapy is prescribed primarily for persons who meet criteria for a diagnosis of Gender Identity Disorder (GID) in adolescents or adults in the *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition, Text Revision (DSM-IV-TR) (APA, 2000) or Transsexualism in the *Diagnostic and Statistical Manual of Mental Disorders,* Third Edition, Revised (DSM-III-R) (APA, 1987). Prescribing hormones for persons not meeting these criteria was called a "deeply controversial" practice in the 1998 version of the HBIGDA *Standards of Care* (Levine et al., 1998, p. 32), but it is clear that many persons who do not meet these criteria nevertheless seek and undergo hormone therapy (Docter & Fleming, 1992; Docter & Prince, 1997; Hage & Karim, 2000). The most recent version of the *Standards of Care* (Meyer et al., 2001) specifically states that hormone therapy can be appropriate for and "can provide significant comfort to" (p. 21) transgender patients who do not wish to live full-time in cross-gender role or who do not desire feminizing or masculinizing surgical procedures; these criteria seem to apply primarily to male cross-dressers. Nearly half of the male cross-dressers surveyed by Docter and Prince (1997) reported an interest in using feminizing hormones; given the prevalence of cross-dressing in the male population, the number of patients potentially interested in feminizing hormone therapy appears to be large.

According to the HBIGDA *Standards of Care* (Meyer et al., 2001), cross-sex hormone therapy is ideally prescribed only on the recommendation of an experienced mental health professional. However, transgender persons frequently acquire and self-administer hormones without such a recommendation and without medical supervision (McGowan, 1999; Xavier, 2000; Clements-Nolle et al., 2001). In response to this phenomenon, the most recent version of the *Standards of Care* (Meyer et al., 2001) authorized prescription of hormones without the recommendation of a mental health professional in selected cases to persons engaged in unsupervised hormone use to encourage medically monitored therapy. This mode of prescribing has been used for many years by clinics that serve large numbers of transgender clients (e.g., the Tom Waddell Health Center in San Francisco) (Tom Waddell Health Center Transgender Team, 2001).

2.2 Feminizing Hormone Therapy in Adults

2.2.1 Administration and Effects of Feminizing Hormone Therapy

Estrogens are the principal medications used to promote feminization in MtF transsexuals and transgender persons. Estrogens induce femi-

nization by binding to estrogen receptors and promote demasculinization by suppressing the release of pituitary gonadotropins, thereby reducing testicular production of testosterone. Estrogens also directly inhibit testosterone production in the testes (Leinonen et al., 1981; Schulze, 1988). Estrogens can be administered orally, by intramuscular injection, or using transdermal patches.

Progesterone or medications with progesterone-like activity (progestagens) are also sometimes prescribed for MtF transgender persons, either to promote breast development or for their antiandrogenic effects. The most frequently prescribed drugs are progesterone, medroxyprogesterone acetate, and cyproterone acetate (CPA); the last of these medications is not available in the United States. Progesterone and progestagens promote the growth of lobules and acinii in breast tissue by binding to progesterone receptors; Kanhai et al. (2000) demonstrated that the use of medications with progesterone-like activity is necessary for the full development of breast histology similar to that of natal women in MtF transsexuals. However, Meyer et al. (1986) could find no appreciable effect of medroxyprogesterone acetate on breast size in MtF transsexuals. Because of their potential risks and uncertain benefits (Moore et al., 2003), progesterone and progestagens are not routinely prescribed for MtF patients (e.g., Tom Waddell Health Center Transgender Team, 2001; Tangpricha et al., 2003; Dittrich et al., 2005).

Antiandrogens are often prescribed in conjunction with estrogens to reduce the dose of estrogen required. In the United States, spironolactone, a medication originally developed as a diuretic, is probably the most commonly prescribed antiandrogen; it promotes demasculinization by reducing testosterone production, inhibiting the conversion of testosterone to its active metabolite dihydrotestosterone (DHT), and blocking the effects of testosterone and DHT at tissue receptors (Prior et al., 1989). Outside the United States, CPA is often prescribed for its antiandrogenic effects (e.g., Jequier et al., 1989; Asscheman & Gooren, 1992). Gonadotropin-releasing hormone (GnRH) agonists, such as gosserelin, triptorelin, and leuprolide, reduce testosterone levels by suppressing the production of pituitary gonadotropins and are sometimes prescribed for their antiandrogenic effects (Dittrich et al., 2005).

Desirable effects of feminizing hormone therapy include breast growth (Orentreich & Durr, 1974; Kanhai et al., 2000b), redistribution of body fat to a more female-typical pattern (Elbers et al., 1999), increased subcutaneous fat and decreased muscle mass (Elbers et al., 1997, 1999), softening of the skin (Schlatterer et al., 1996), reduction in the rate of growth of facial and body hair (Giltay & Gooren, 2000), reduction or cessation of scalp hair loss, decreased testicular size (Meyer et al., 1986), and reduction or elimination of spontaneous erections (Kwan et al., 1985). Feminizing hormone therapy has no appreciable effect on vocal pitch or penile length (Meyer et al., 1986). Bone mineral density is well preserved and also increases (van Kesteren et al., 1996a, 1998; Reutrakul et al., 1998; Schlatterer et al., 1998a; Sosa et al., 2003; Mueller et al., 2005). Reported side effects of feminizing hormone therapy include weight gain (Elbers et al., 1997, 1999), galactorrhea (fluid discharge from the nipples) (Gooren et al., 1985; Schlatterer

et al., 1998b), decreased red cell mass (Rosenmund et al., 1988; Schlatterer et al., 1998b), decreased libido (van Kemenade et al., 1989; van Goozen et al., 1995; Schlatterer et al., 1996), and infertility (Lübbert et al., 1992). Most hormone-induced changes are reversible if feminizing hormones are discontinued, but breast growth must be assumed to be permanent. The time course and permanence of the testicular changes leading to reduced testosterone production and infertility are incompletely understood. Testosterone response to gonadotropin challenge can disappear after a period of estrogen treatment as short as 13 months but has been observed after a period of treatment as long as 25 months (Futterweit et al., 1984). Cessation of feminizing hormone therapy after 140 days of treatment has been observed to result in complete recovery of sperm counts and sperm quality (Lübbert et al., 1992).

Feminizing hormones have emotional and psychological effects in addition to inducing physical changes. Early observers noted that feminizing hormones had a calming effect in MtF transsexuals and seemed to act as a "biotranquilizer" (Block & Tessler, 1971, p. 518). Leavitt et al. (1980) found that a group of MtF transsexuals taking feminizing hormones displayed better psychological adjustment than a comparable group not using hormones and that, in the hormone-using group, greater duration of hormone use was associated with better psychological adjustment. Cohen-Kettenis and Gooren (1992) concluded that in MtF transsexuals "the main effect of estrogen seems to be one of calming down emotional turbulences" (p. 63). Van Kemenade et al. (1989) observed that antiandrogen treatment increased feelings of relaxation and energy in MtF transsexuals. Slabbekoorn et al. (2001) reported that feminizing hormone therapy increased the intensity of positive emotions in MtF transsexuals; nonverbal emotional expressivity also increased. Asscheman et al. (1989) found an increased prevalence of depressive mood changes in association with feminizing hormone therapy, but T'Sjoen et al. (2004) have questioned whether this finding is attributable to hormone therapy.

Medical treatments that result in loss of fertility are usually preceded by a discussion of reproductive consequences and options, and feminizing hormone therapy should be no exception (Lawrence et al., 1996; De Sutter, 2001). The HBIGDA *Standards of Care* (Meyer et al., 2001) state that MtF transsexuals should be counseled about reproductive options, including cryopreservation (freezing and banking) of sperm, before beginning feminizing hormone therapy. In an Internet survey, a significant number of MtF transsexuals expressed an interest in sperm cryopreservation before beginning hormone therapy (De Sutter et al., 2003).

2.2.2 Complications of Feminizing Hormone Therapy

One report from the Netherlands found an increased mortality rate among hormone-treated MtF transsexuals (Asscheman et al., 1989), but this finding was not confirmed in a later study in the same population (van Kesteren et al., 1997). Feminizing hormone therapy is associated with potentially serious medical complications, including an increased risk of developing blood clots (venous thrombosis and pulmonary embolism) (van Kesteren et al., 1997), gallstones (van Kesteren et al.,

1997), liver disease (Meyer et al., 1986; van Kesteren et al., 1997; Tangpricha et al., 2001), pancreatitis (Perego et al., 2004), insulin resistance (Polderman et al., 1994) and glucose intolerance (Feldman, 2002), and elevated prolactin levels (van Kesteren et al., 1997), rarely accompanied by pituitary enlargement or the development of prolactin-secreting pituitary tumors called prolactinomas.

The most significant complications of feminizing hormone therapy are related to the development of venous thrombosis and pulmonary embolism. Van Kesteren et al. (1997) found that in a group of 816 MtF transsexual patients treated with oral CPA and either oral ethinyl estradiol (a potent synthetic estrogen) or transdermal estradiol, 45 patients (5.5%) experienced venous thrombosis or pulmonary embolism, a percentage more than 19 times that observed in the general population. Most thromboembolic events occurred during the first 12 months of treatment, and all but one occurred in persons taking ethinyl estradiol. Oral ethinyl estradiol appears to be significantly more thrombogenic than either oral or transdermal estradiol: Toorians et al. (2003) found that MtF transsexual patients treated with CPA and oral ethinyl estradiol showed significantly greater changes in hemostatic variables, especially resistance to the anticoagulant factor *activated protein C*, than patients treated with CPA and transdermal estradiol, CPA and oral estradiol, or CPA alone. Patients in the last three groups showed similar and relatively minor changes in hemostatic variables. These results suggest that the high prevalence of venous thrombosis and pulmonary embolism observed in MtF patients treated with oral ethinyl estradiol (van Kesteren et al., 1997) was probably related more to the specific chemical structure of ethinyl estradiol than to oral administration of estrogen per se (Toorians et al., 2003). However, data from natal women receiving postmenopausal estrogen replacement therapy suggest that transdermal estrogen is associated with a significantly lower risk of venous thromboembolism than oral estrogen (Scarabin et al., 2003).

The risks of estrogen-induced thrombosis may be increased in men and MtF transgender persons with known cardiovascular disease. In the Coronary Drug Project, conducted during the 1960s in middle-aged men with one or more previous myocardial infarctions, treatment with oral conjugated estrogens in dosages comparable to those used in MtF transsexuals resulted in a significantly increased incidence of venous thrombosis and pulmonary embolism relative to a placebo-treated group (Coronary Drug Project Research Group, 1970).

Postmenopausal estrogen therapy in natal women carries an increased risk of stroke (Women's Health Initiative Steering Committee, 2004) and postmenopausal therapy with an estrogen-progestagen combination carries an increased risk of both coronary heart disease and stroke (Writing Group for the Women's Health Initiative Investigators, 2002). Surprisingly, however, feminizing hormone therapy has not been demonstrated to increase the risk of either stroke or myocardial infarction in MtF transsexuals (van Kesteren et al., 1997). Feminizing hormone therapy appears to offer some cardiovascular benefits to MtF transsexuals, which plausibly may counterbalance the undesirable thrombogenic effects of estrogens and progestagens. For example, in comparison with untreated men, estrogen-treated MtF transsexuals

demonstrated greater arterial reactivity following arterial occlusion or nitroglycerine infusion (McCrohon et al., 1997; New et al., 1997), which may confer cardioprotective benefits in persons with atherosclerosis. Estrogen treatment in MtF transsexuals also reduces levels of homocysteine (Giltay et al., 1998), a known risk factor for cardiovascular disease.

Estrogen treatment in MtF transsexuals appears to shift lipid profiles toward a more female-typical pattern, potentially reducing cardiovascular risk. Relative to male controls, estrogen-treated MtF transsexuals have been observed to have significantly lower total cholesterol (TC)/high-density lipoprotein cholesterol (HDL-C) ratios (Damewood et al., 1989), higher levels of HDL-C and lower levels of low-density lipoprotein cholesterol (LDL-C) (New et al., 1997; Elbers et al., 2003), and lower levels of TC and LDL-C (Sosa et al., 2004). McCrohon et al. (1997), however, found no difference in TC or HDL-C between estrogen-treated MtF transsexuals and untreated men. Not all reported effects of feminizing hormones on lipid profiles are positive. Elbers et al. (2003) reported that treatment with estrogen and CPA increased triglyceride levels in MtF transsexuals, and New et al. (1997) found that estrogen-treated MtF transsexuals had somewhat higher triglyceride levels than untreated men.

Elevated prolactin levels are observed in many MtF transsexuals treated with feminizing hormone therapy (van Kesteren et al., 1997). Moderate elevations of prolactin are not of concern, but prolactin levels that persistently exceed about three times the upper limit of normal have occasionally been associated with pituitary enlargement (Asscheman et al., 1988) or rarely with development of prolactin-secreting tumors (prolactinomas) (Gooren et al., 1988; Kovacs et al., 1994; Serri et al., 1996; Futterweit, 1998). Loss of peripheral vision due to compression of the optic nerves, a potential complication of pituitary enlargement or prolactinoma, has apparently never been reported in estrogen-treated MtF transsexuals.

2.3 Masculinizing Hormone Therapy in Adults

2.3.1 Administration and Effects of Masculinizing Hormone Therapy

Testosterone is usually the only medication prescribed to induce masculinization in FtM transsexuals and transgender persons. It is typically administered by intramuscular (IM) injection at a dosage of about 200 mg every 2 weeks. Testosterone induces masculinization by binding to androgen receptors. Theoretically, it should also contribute to defeminization by suppressing the release of pituitary gonadotropins, thereby reducing ovarian production of estrogen and progesterone. However, suppression of gonadotropin production is often incomplete with moderate doses of testosterone (e.g., 300 mg IM per month) (Zwirska-Korczala et al., 1996), although significant suppression is usual with larger doses (e.g., 500 mg IM per month) (Spinder et al., 1989). Because testosterone undergoes peripheral conversion to estradiol, estradiol levels in FtM transsexuals often remain within the normal female range, both before and after ovariectomy (Spinder et al., 1989; Elbers et al., 1997). Although testosterone is usually administered by IM injection, transdermal preparations (patches and gel) are also available.

Transdermal testosterone is more expensive than injectable testosterone, appears to induce masculinization more slowly (Tangpricha et al., 2003), and is probably less effective for suppressing menses; consequently, it is usually prescribed only for persons who seek limited masculinization or for maintenance therapy following initial masculinization with injectable testosterone in persons who have undergone hysterectomy and ovariectomy (Oriel, 2000). Oral testosterone is rarely prescribed in the United States because available preparations are hepatotoxic in the dosages needed for masculinizing therapy (Rhoden & Morgentaler, 2004). Progesterone is occasionally prescribed along with testosterone to help suppress menses (Schlatterer et al., 1996; Gooren, 1999).

Testosterone therapy typically results in deepening of the voice (Meyer et al., 1986), enlargement of the clitoris (Meyer et al., 1986), increased muscle mass and decreased subcutaneous fat (Elbers et al., 1997, 1999), slight reduction in breast size (Meyer et al., 1986), increased facial and body hair (Schlatterer et al., 1996), male pattern scalp hair loss (Giltay et al., 2004), and cessation of menses (Meyer et al., 1986; Schlatterer et al., 1996). Some of these changes are reversible if testosterone is discontinued, but voice deepening, clitoral enlargement, facial and body hair changes, and scalp hair loss must be assumed to be permanent.

Masculinizing hormone therapy has emotional and psychological effects in addition to its physical effects. Van Goozen et al. (1995) observed increases in aggressiveness, anger-proneness, and sexual interest and arousability in testosterone-treated FtM transsexuals. Slabbekoorn et al. (2001) found that masculinizing hormone therapy decreased the intensity of both positive and negative emotions in FtM transsexuals but increased anger-readiness and frequency of sexual feelings and behaviors. Perrone et al. (2003) observed decreased feelings of depression and increased sexual interest and arousability following testosterone therapy in FtM transsexuals. In a large Internet-based survey of self-identified FtM transgender persons, Newfield et al. (in press) found that testosterone use was associated with higher quality-of-life scores in domains related to social functioning and overall mental health.

The HBIGDA *Standards of Care* (Meyer et al., 2001) state that FtM transsexuals should be counseled about reproductive considerations before beginning masculinizing hormone therapy. At present, embryo cryopreservation is the only practical fertility preservation option available to FtM transsexuals, but ovarian tissue banking may become practical in the future (De Sutter, 2001).

2.3.2 Complications of Masculinizing Hormone Therapy

Masculinizing hormone therapy has not been shown to be associated with increased mortality (van Kesteren et al., 1997). However, side effects and complications of masculinizing hormone therapy have been reported; they include acne (van Kesteren et al., 1997), weight gain (Elbers et al., 1997), increased red cell mass with possible polycythemia (Futterweit, 1998), liver disease (van Kesteren et al., 1997), insulin resistance (Polderman et al., 1994), fluid retention and edema (van Kesteren et al., 1997; Futterweit, 1998), increases in plasma homo-

cysteine levels (Giltay et al., 1998), decreases in arterial reactivity (McCredie et al., 1998), and shift of lipid profiles toward a more male-typical pattern (Meyer et al., 1986; McCredie et al., 1998; Elbers et al., 2003; Giltay et al., 2004) with the potential for increased cardiovascular risk. Elevated prolactin levels have occasionally been reported in FtM transsexuals and may be attributable to breast binding (Schlatterer et al., 1998b).

Testosterone treatment typically produces changes in ovarian histology similar to those observed in women with polycystic ovarian syndrome (Futterweit & Deligdisch, 1986; Spinder et al., 1989). The significance of this finding is uncertain, especially as untreated FtM transsexuals often have elevated testosterone levels (Futterweit et al., 1986; Bosinski et al., 1997) and polycystic ovaries (Futterweit et al., 1986; Balen et al., 1993; Bosinski et al., 1997). Gooren (1999) observed that polycystic ovaries were more likely to undergo malignant changes and consequently recommended that testosterone-treated FtM transsexuals undergo ovariectomy soon after successful transition to the male gender role.

Bone mineral density in testosterone-treated FtM transsexuals is generally well preserved prior to ovariectomy (van Kesteren et al., 1996a; Goh & Ratnam, 1997) and following ovariectomy if testosterone is taken regularly and in adequate dosage (Lips et al., 1996; Goh & Ratnam, 1997). However, decreases in bone mineral density following ovariectomy have been reported in FtM transsexuals who stop taking testosterone or use testosterone irregularly (Goh & Ratnam, 1997) or in whom testosterone dosage is not high enough to suppress luteinizing hormone (LH), a gonadotropin (van Kesteren et al., 1998). Van Kesteren et al. (1998) proposed that measuring serum LH may be a better indicator of the adequacy of testosterone dosage for preservation of bone mass in FtM transsexuals following ovariectomy than measuring testosterone itself.

Greenman (2004) and Michel et al. (2001) expressed concerns about endometrial hyperplasia, which may be a risk factor for endometrial carcinoma, in testosterone-treated FtM transsexuals. These concerns apparently derive from a report of three instances of mild hyperplasia observed following hysterectomy among 19 testosterone-treated FtM patients (Futterweit & Deligdisch, 1986); no information was provided about estradiol levels in these patients. Chadha et al. (1994) and Miller et al. (1986) detected no instances of endometrial hyperplasia in their respective series of 6 and 32 testosterone-treated FtM patients. Futterweit (1998) asserted that the risks associated with possible endometrial hyperplasia in testosterone-treated FtM patients were such that hysterectomy should be performed "at the earliest possible time" (p. 217) consistent with the patient's psychological and clinical progress, an opinion shared by Michel et al. (2001).

2.4 Hormone Therapy in Transgender Adolescents

It is not unusual for adolescents with GID to seek cross-sex hormone therapy (Cohen-Kettenis & Pfäfflin, 2003). Such requests pose dilemmas

for caregivers, parents, and transsexual adolescents themselves. Some adolescents with GID will not sustain the wish to live as members of the opposite sex into adulthood (Meyenburg, 1999), which would argue against the provision of cross-sex hormone therapy, with its relatively irreversible physical effects, to transgender adolescents. On the other hand, the physical changes of puberty can be extremely distressing to adolescents with GID, and prevention of unwanted masculinization or feminization can also make physical presentation in the desired gender role much easier if the adolescent does decide to live full-time as a member of the opposite sex (Cohen-Kettenis & Pfäfflin, 2003).

One option for the treatment of adolescents with GID is to prescribe puberty-blocking hormones, such as GnRH agonists (Gooren & Delemarre-van de Waal, 1996; Cohen-Kettenis & van Goozen, 1998). GnRH agonists suppress the production of endogenous testosterone in male adolescents and the production of estrogen and progesterone in female adolescents, thereby preventing irreversible masculinization or feminization. Puberty-blocking hormones thus give adolescents time to consider their options. If living full-time in the opposite gender role is still desired in adulthood, feminizing or masculinizing hormones can be prescribed; if not, puberty-blocking hormones can be discontinued and normal puberty will occur. Since 1998, the HBIGDA *Standards of Care* have authorized the prescription of puberty-blocking hormones for selected transgender adolescents (Levine et al., 1998; Meyer et al., 2001).

Carefully selected adolescents with GID who are allowed to begin the sex reassignment process during adolescence, including administration of puberty-blocking hormones in some cases, experience relief of gender dysphoria, high levels of satisfaction, and good psychological functioning following sex reassignment (Cohen-Kettenis & van Goozen, 1997; Smith et al., 2001). At present it is unclear which adolescents with GID are the most appropriate candidates for puberty-blocking hormones. Cohen-Kettenis and Pfäfflin (2003) proposed that their use should be limited to those gender-dysphoric adolescents who had consistently manifested extreme cross-gender behavior since childhood, who clearly desired to adopt the social role of the opposite sex, whose gender dysphoria had increased significantly with the onset of puberty, who displayed minimal or no comorbid psychopathology, and whose parents consented and were cooperative. Zucker (2001) observed, however, that limiting puberty-blocking hormones to persons without significant coexisting psychopathology was likely to exclude the "vast majority" (p. 2086) of gender-dysphoric adolescents and that the issue was further complicated by the possibility that comorbid psychopathology can sometimes be a direct consequence of chronic gender dysphoria. He proposed that randomized controlled trials would help clarify whether coexisting psychopathology is an appropriate exclusion criterion for puberty-blocking hormones.

2.5 Use of Nonprescribed and Unsupervised Hormones

Many transgender persons use nonprescribed cross-sex hormones obtained from friends, black market sources, or suppliers in foreign countries. In a survey conducted in Washington, DC, 58% of a com-

bined group of MtF and FtM transgender persons reported having used nonprescribed hormones (Xavier, 2000). In a New York City survey, 39% of MtF transsexuals and 9% of FtM transgender persons reported using nonprescribed hormones (McGowan, 1999); and in a San Francisco survey, the figures were 29% for MtF transgender persons and 3% for FtM transgender persons (Clements-Nolle et al., 2001). Dosages of nonprescribed hormones often exceed those typically prescribed by physicians. Moore et al. (2003) found that 28% of presurgical MtF patients presenting at a gender clinic reported using hormone dosages more than three times greater than what is typically prescribed, although hormone dosages used by FtM patients were in an appropriate range. Despite the apparent widespread use of nonprescribed hormones and the high dosages frequently employed, there is little information available concerning complications of this practice.

Notwithstanding the potential risks, many transgender persons are willing to use nonprescribed hormones to achieve the physical and psychological changes they desire. The benefits of nonprescribed hormones can be genuine. For example, Leavitt et al. (1980) reported that MtF transsexuals who used medically unsupervised hormones displayed better psychological adjustment than transsexuals who were not receiving hormone treatment.

3 Surgical Treatment for Transgender Persons

3.1 Surgical Treatment for Male-to-Female Transsexuals

The desire for feminizing genitoplasty, usually called MtF "sex reassignment surgery" (SRS), is arguably the defining characteristic of MtF transsexuals. SRS been performed in MtF transsexuals for more than 70 years (Karim et al., 1996) and has reached a high state of technical refinement. In expert hands, it yields excellent cosmetic and functional results and highly favorable subjective outcomes (Green & Fleming, 1990; Muirhead-Allwood et al., 1999; Lawrence, 2003). MtF SRS usually involves orchiectomy, penectomy, vaginoplasty, and vulvoplasty. Typically the neovagina is lined with the inverted skin of the penis (penile inversion vaginoplasty); this is widely regarded as the technique of choice for MtF SRS (Karim et al., 1996; Giraldo et al., 2002). Most surgeons construct a sensate clitoris from a portion of the glans penis, a technique that is "recognized today as the best choice for neoclitoroplasty" (Giraldo et al., 2002, p. 1308).

Although all elements of the sex reassignment process contribute to relief of gender dysphoria (Kuiper & Cohen-Kettenis, 1988), MtF SRS appears to provide particular psychological and social benefits. In a randomized, controlled, prospective study of MtF SRS outcomes, Mate-Kole et al. (1990) observed that, in comparison to a wait-list control group, MtF patients who underwent SRS on an expedited basis experienced better psychosocial outcomes, displaying fewer neurotic symptoms and greater engagement in social activities. Satisfaction following MtF SRS is extremely high, and MtF transsexuals rarely express regret after undergoing SRS. In two large SRS follow-up surveys ($n = 140$ and 232, respectively), no respondents reported outright regret, and only

6% expressed even occasional regret, which often was unrelated to SRS per se (Muirhead-Allwood et al., 1999; Lawrence, 2003).

Potential complications of MtF SRS include vaginal stenosis, genital pain, clitoral necrosis, urethral stenosis, and rectovaginal or vesicovaginal fistulas (Krege et al., 2001; Lawrence, in press). Not surprisingly, good surgical results and lack of complications are usually associated with higher levels of subjective satisfaction and better psychosocial outcomes (Ross & Need, 1989; Muirhead-Allwood et al., 1999; Schroder & Carroll, 1999; Lawrence, 2003, in press).

MtF SRS performed in North America typically costs between $15,000 and $20,000 and is usually not covered by health insurance policies in the United States; this makes SRS prohibitively expensive for many patients. Some MtF transsexuals who cannot afford SRS undergo only orchiectomy, a much less expensive procedure that eliminates testosterone production by the testes and allows lower dosages of feminizing hormones to be used (Israel & Tarver, 1997).

Because they often feel that hormone-induced breast development is inadequate, many MtF transsexuals and transgender persons undergo augmentation mammaplasty (breast-enlargement surgery). In the Netherlands, about two thirds of MtF transsexuals who undergo vaginoplasty also undergo augmentation mammaplasty (Kanhai et al., 2001). Approximately 75% of patients express satisfaction after augmentation mammaplasty; the most frequent complaint by dissatisfied patients is that their breasts were not made large enough (Kanhai et al., 2000).

3.2 Surgical Treatment for Female-to-Male Transsexuals

Reduction mammaplasty, often referred to as chest reconstruction, is the surgical procedure most frequently sought by FtM transsexuals and transgender persons. The principal techniques and aesthetic considerations are outlined by Hage and van Kesteren (1995). Even with careful placement and orientation of incisions, scar revisions are frequently required following FtM chest reconstruction. Newfield et al. (in press) found that FtM transgender persons who had undergone chest reconstruction reported higher quality-of-life scores in domains related to general health, social functioning, and mental health.

In contrast to the situation in MtF transsexuals, there are currently no entirely satisfactory masculinizing genitoplasty techniques available to FtM transsexuals, which led Green and Fleming (1990) to conclude that "those [FtMs] with a weak interest in [phalloplasty] have a better prognosis" (p. 172). A variety of FtM genitoplasty techniques are available, but two have achieved the widest acceptance. In *metoidioplasty* (sometimes spelled *metaidoioplasty*), the hypertrophied clitoris is released from its suspensory ligament, creating a microphallus that retains sexual sensation; urethral lengthening can also be performed if desired (Hage, 1996). The small size of the resulting phallus is the principal disadvantage of this technique. In *radial forearm flap phalloplasty* (e.g., Gottlieb et al., 1999; Rohrmann & Jakse, 2003), a free flap of skin from the forearm is used to create a tube-within-a-tube neophallus that permits standing voiding and that often has both protective and sexual

sensation. Sometimes a hydraulic penile prosthesis can be inserted to achieve rigidity (Hoebeke et al., 2003). Major disadvantages of the radial forearm flap technique include frequent urethral stenoses and fistulas (Rohrmann & Jakse, 2003), unattractive donor site healing, and formidable expense. De Cuypere et al. (2005) observed the FtM phalloplasty patients who received hydraulic penile prostheses displayed a trend toward greater realization of their sexual expectations than patients who did not, but were also more likely to report pain during intercourse. With both metoidioplasty and phalloplasty, the labia majora are usually brought together to create a neoscrotum in which testicular prostheses are inserted (Sengezer & Sadove, 1993). Because there is significant room for improvement in current techniques, masculinizing genitoplasty procedures will continue to evolve.

4 Screening for Neoplasia in Hormone-Treated Transgender Persons

It is not known whether cross-sex hormone therapy affects the incidence of neoplasia in transgender persons; however, case reports of neoplasia in transgender persons treated with cross-sex hormones are uncommon. Case reports in MtF transsexuals include five breast carcinomas (Symmers, 1968; Pritchard et al., 1988; Ganly & Taylor, 1995; Grabellus et al., 2005), two breast fibroadenomas (Kanhai et al., 1999; Lemmo et al., 2003), four prolactinomas (Gooren et al., 1988; Kovacs et al., 1994; Serri et al., 1996; Futterweit, 1998), four prostatic carcinomas (Markland, 1975; Thurston, 1994; Gooren et al., 1997; van Haarst et al., 1998), one neovaginal carcinoma (Harder et al., 2002), and one case of neovaginal intraepithelial neoplasia (Lawrence, 2001). Case reports in FtM transsexuals include three ovarian carcinomas (Hage et al., 2000; Dizon et al., 2006), one cervical carcinoma (Driak & Samudovsky, 2004), and two cases of breast carcinoma in residual breast tissue following mastectomy (Gooren, 1999; Burcombe et al., 2003). In these cases, there may be a plausible causal link with cross-sex hormone therapy. In addition, van Kesteren et al. (1997) observed seven cancer deaths in MtF transsexuals (three cases of pulmonary carcinoma, one case each of gastric carcinoma, leukemia, glioblastoma, and meningioma) and one cancer death in a FtM transsexual (from colon carcinoma); in these cases a possible causal link with cross-sex hormone therapy is not obvious.

The HBIGDA *Standards of Care* (Meyer et al., 2001) state that transgender patients, "whether on hormones or not, should be screened for pelvic malignancies as are other persons" (p. 23), but there are no data to suggest what screening techniques or intervals might be optimal. The *Standards of Care* recommendations imply that FtM transsexuals who have not undergone hysterectomy should have periodic Pap smears performed (Moore et al., 2003; Tangpricha et al., 2003), although Greenman (2004) suggested that this may not always be necessary. Testosterone treatment is associated with cervical mucosal atrophy in many cases, which can result in a misdiagnosis of cervical dysplasia (Miller et al., 1986). Moore et al. (2003) proposed that testosterone-treated FtM transsexuals should

also undergo regular uterine ultrasonography examinations to detect endometrial hyperplasia, a risk factor for endometrial carcinoma.

There is disagreement as to whether MtF transsexuals who have undergone penile inversion vaginoplasty should be screened for neovaginal cancer with Pap smears. Kirk (2001) argued that regular screening Pap smears were indicated for MtF transsexuals following vaginoplasty. Lawrence (2001) observed that if MtF transsexuals were screened for pelvic malignancies according to the recommendations for natal women, then vaginal Pap smears would not be indicated because they are not recommended for natal women who lack a cervix and who have no history of cancer or abnormal cytology (American Academy of Family Physicians, 2004). Vaginal and neovaginal cancers are rare, and vaginal Pap smears lack sensitivity and specificity; consequently, most positive Pap smears from MtF transsexuals would be false positives. Annual pelvic examination without routine Pap smears probably provides optimal screening for most MtF transsexuals who have undergone penile inversion vaginoplasty; exceptions might be patients in whom penile glans tissue was inverted along with penile skin (nowadays an uncommon practice) because of a possible increased potential for malignancy in glans tissue (Lawrence, 2001).

According to the *Standards of Care* (Meyer et al., 2001), hormone-treated MtF transsexuals should be monitored for prostate and breast cancer, but there are no data demonstrating the benefits of such monitoring. The value of prostate-specific antigen (PSA) screening in MtF transsexuals appears to be especially doubtful: PSA testing has not been shown to be beneficial in natal males (Harris & Lohr, 2002), and estrogen strongly suppresses PSA levels in MtF transsexuals (Jin et al., 1996; van Kesteren et al., 1996b).

It is unclear whether monitoring for breast cancer in MtF transsexuals should include mammography, and which if any transsexuals might benefit from it. Feldman and Bockting (2003) recommended annual "mammograms starting at age 40 for patients on hormones who have even modest breast development" (p. 31); Tangpricha et al. (2003) suggested that "mammography may be indicated in high-risk [MtF] patients" (p. 16); and Moore et al. (2003) advised considering mammography for MtF patients over age 50. However, MtF transsexuals are likely to have had many fewer years of estrogen exposure, a known risk factor for breast cancer (Dunn et al., 2005), than natal women of similar age, which might argue against routine mammography for most MtF transsexuals. The potential benefits of mammography must be balanced against the risks of false-positive results and overdiagnosis. Most MtF transsexuals take estrogen indefinitely, and current or recent estrogen use significantly increases the likelihood of false positive mammography (Banks et al., 2004). The problem of overdiagnosis—detection of lesions of low malignant potential that would otherwise not have come to clinical attention during the person's lifetime—is also significant when screening mammography is performed in older persons: Zahl et al. (2004) estimated that in Norway and Sweden one-third of invasive breast cancers detected with screening mammography in persons 50 to 69 years old were overdiagnosed. Moreover, many MtF transsexuals undergo breast augmentation (Kanhai et al., 2001), which lowers the sen-

sitivity of screening mammography in natal women (Miglioretti et al., 2004); mammography in persons who have undergone breast augmentation also carries a small risk of implant rupture (Brown et al., 2004).

The *Standards of Care* state that hormone-treated FtM transsexuals who have "undergone mastectomies and who have a family history of breast cancer should be monitored for this disease" (Meyer et al., 2001, p. 23). Although testosterone is not believed to induce premalignant changes in breast tissue (Burgess & Shousha, 1993), detection of carcinoma in residual breast tissue following mastectomy in two FtM transsexuals (Gooren, 1999; Burcombe et al., 2003) suggests that periodic breast examinations would be prudent in all FtM transgender persons.

5 Liquid Silicone Injection in Transgender Persons

Some MtF transgender persons undergo subcutaneous injection of liquid silicone in an attempt feminize their appearance. The hips and buttocks are the areas most frequently injected (Hage et al., 2001); other reported sites include the face, breasts, and legs. Silicone injection, which may be performed by medical personnel or, more often, by nonmedical practitioners, is seen by some MtF transgender persons as a quick, inexpensive alternative to conventional cosmetic surgical procedures. The total volume injected can be up to 8 liters (Hage et al., 2001), typically over multiple sessions (Wiessing et al., 1999). Occasionally, other viscous fluids, such as mineral oil or olive oil, are injected or are combined with silicone. In some urban areas such as New York City, silicone injection occurs frequently enough to have been called "epidemic" (Fox et al., 2004, p. 452). In a New York City survey of MtF transsexuals, 11% reported receiving silicone injections from professional providers and 18% from "black market" providers (McGowan, 1999). In Rotterdam, Wiessing et al. (1999) found that more than half of transgender street prostitutes surveyed had received silicone injections to the face, breasts, thighs, or buttocks; on average, they had received injections about twice a year.

Liquid silicone injection has been associated with a variety of devastating complications. Embolism of silicone to the lungs can cause acute pneumonitis, leading to severe respiratory distress (e.g., Duong et al., 1998; Kim et al., 2003; Rosioreanu et al., 2004) or death (Ellenbogen & Rubin, 1975; Rodriguez et al., 1989). Pneumonitis typically occurs within hours or a few days of injection but has been observed up to months (Duong et al., 1998) or years after injection, sometimes following trauma (Chastre et al., 1987). Acute silicone pneumonitis has been reported after injection of volumes as small as 10 cc (Kim et al., 2003).

Facial injection of liquid silicone has been associated with the development of granulomatous reactions and cellulitis (Bigatà et al., 2001) and loss of vision (Shin et al., 1988). Silicone-related granulomatous hepatitis has been described (Ellenbogen & Rubin, 1975). Liquid silicone is affected by gravity and can migrate in the body, sometimes resulting in severe disfigurement and disability (Hage et al., 2001). Injection or migration of silicone into the legs can cause chronic ulceration (Rae et al., 1989) and lymphedema (Gaber, 2004), often after a

latent period of many years. Multiple cases of *Mycobacterium abscessus* infection have been reported in New York City following liquid silicone injection (Fox et al., 2004). In view of the severity of associated complications, transgender persons should be strongly counseled to avoid liquid silicone injections (Hage et al., 2001).

6 HIV/AIDS and Other Sexually Transmitted Infections in Transgender Persons

Some groups of MtF transgender persons in the United States have disproportionately high HIV seropositivity prevalences and seroconversion rates. Reported HIV seropositivity prevalences from studies conducted with convenience samples of MtF transgender persons include these figures: 25% in New York City (McGowan, 1999); 19% in Philadelphia (Kenagy, 2002); 48%, 35%, and 16% in San Francisco (Nemoto et al., 1999; Clements-Nolle et al., 2001; Kellogg et al., 2001); 32% in Washington, DC (Xavier, 2000); and 22% in Los Angeles (Simon et al., 2000). In comparison, the estimated overall prevalence of HIV infection among U.S. adolescents and adults in 2003 was 0.13% (Centers for Disease Control and Prevention, 2004). Factors associated with HIV seropositivity in MtF transgender persons include lower levels of income and education (Simon et al., 2000), African American ethnicity, nonhormonal injection drug use, and large numbers of lifetime sexual partners (Clements-Nolle et al., 2001). Very high seroconversion rates have also been reported in some samples of MtF transgender persons: 3.4 per 100 person-years in a Los Angeles study (Simon et al., 2000) and 7.8 per 100 person-years in a San Francisco study (Kellogg et al., 2001). In the study by Kellogg et al. (2001), factors associated with higher seroconversion rates included African American ethnicity and engaging in receptive anal sex.

HIV seropositivity is especially high among MtF transgender persons who engage in sex work and in MtF persons of color, especially African Americans. In a study of MtF transgender sex workers in Atlanta (more than 80% of whom were African American), 68% were HIV seropositive (Elifson et al., 1993). In a sample of MtF transgender persons of color in San Francisco, all of whom had a history of exchanging sex for money or drugs, Nemoto et al. (2004) found an overall HIV seropositivity prevalence of 26%, with seropositivity significantly associated with engaging in unprotected receptive anal sex with casual partners. African Americans had the highest HIV seropositivity prevalence, 41%, followed by Latinas, 23%, and Asians/Pacific Islanders, 13% (Nemoto et al., 2004).

Reported HIV seropositivity prevalence figures in FtM transgender persons are much lower than among MtF persons: 0% in Philadelphia and New York City (McGowan, 1999; Kenagy, 2002), 2% in San Francisco (Clements-Nolle et al., 2001), and 5% or less in Washington, DC (Xavier, 2000).

MtF transgender persons also report a high lifetime prevalence of STIs other than HIV/AIDS. Kenagy (2002) found that 41% of a con-

venience sample of MtF transgender persons reported having been diagnosed with an STI other than HIV/AIDS at some time in their lives; among FtM transgender persons, only 6% reported this. In comparison, in a national probability sample of U.S. adults, about 17% reported having had an STI other than HIV (Laumann et al., 1994). In a survey of MtF transgender persons of color, 14% reported having had an STI other than HIV/AIDS during the past 12 months (Nemoto et al., 2004); among all U.S. adults, the comparable figure was about 1.6% (Laumann et al., 1994).

7 Mental Health Concerns of Transgender Persons

7.1 Transgenderism as a Mental Disorder

Four diagnoses in the DSM-IV-TR (APA, 2000) are specifically applicable to transgender persons; all of these diagnoses require the presence of clinically significant distress or disability, which implies that transgender identity or behavior per se is not sufficient for the diagnosis of a mental disorder under the DSM-IV-TR. The diagnoses of GID in Children and GID in Adolescents or Adults are usually reserved for severely gender-dysphoric persons who are seeking treatment under the HBIGDA *Standards of Care* (Meyer et al., 2001). The diagnosis of Transvestic Fetishism could be applicable to some cross-dressers who experience distress or disability associated with cross-dressing. Gender Identity Disorder Not Otherwise Specified (GIDNOS), the broadest of the four DSM-IV-TR diagnoses, could be applicable to other transgender persons who experience sufficient distress or disability to meet diagnostic criteria.

There is disagreement among transgender persons and their caregivers concerning the value of these DSM diagnostic categories. Some believe that the diagnoses unnecessarily pathologize behavior that may be deviant but that is not pathologic per se, thereby inviting stigmatization of transgender persons (Lev, 2004). Others argue that medical diagnoses such as GID and GIDNOS are needed to justify the provision of medical and surgical services that transsexuals and other transgender persons seek (Meyer et al., 2001). However one may feel about these diagnoses, their presence in the DSM is a reminder that the central mental health concern for many transgender persons, and the issue that underlies many other transgender health concerns, is the suffering associated with gender dysphoria, especially the profoundly distressing sense of "wrong embodiment" (Prosser, 1998, p. 69) that transsexuals experience.

7.2 Other Mental Health Concerns in Transgender Persons

There is conflicting evidence concerning the prevalence of other mental health problems in transgender persons, with some studies reporting elevated levels of psychopathology relative to population norms and others reporting few or no differences. Interpretation of the evidence is complicated by the small sample sizes of many studies and by method-

ologic problems, such as averaging of pooled scores from the Minnesota Multiphasic Personality Inventory (MMPI) or assigning psychiatric diagnoses without the use of standardized interviews or instruments.

Many investigators have used the MMPI to assess mental health in transgender persons. Results have been inconsistent: Cole et al. (1997) and Hunt et al. (1981) found both MtF and FtM transsexuals to be, for the most part, "notably free of psychopathology" (Cole et al., 1997, p. 13) based on MMPI results; Miach et al. (2000), Michel et al. (2002), and Tsushima and Wedding (1979) reached similar conclusions in studies of MtF transsexuals. However, Beatrice (1985) and Langevin et al. (1977) reported significant psychopathology in some MtF transsexuals based on MMPI studies, as did Fleming et al. (1981) in both MtF and FtM transsexuals; the most common findings included antisocial tendencies, thought disorder, or hypomania. MMPI data suggest, however, that transsexuals tend to experience less psychopathology than transgender persons who meet criteria for the DSM-III-R diagnosis of Gender Identity Disorder of Adolescence and Adulthood, Nontranssexual Type (GIDAANT) (Miach et al., 2000; Michel et al., 2002). MMPI data also suggest that mental health typically improves following gender transition in MtF transsexuals (Langevin et al., 1977) and following SRS in both MtF and FtM transsexuals (Fleming et al., 1981; but see Beatrice, 1985). Beatrice (1985) found no evidence of psychopathology in a small group of male cross-dressers based on MMPI results.

Conclusions about psychopathology based on assessment using the Derogatis Sexual Functioning Inventory (DSFI) have also been inconsistent. Derogatis et al. (1978) reported that, relative to male norms, MtF transsexuals described more severe current psychological symptoms, especially depression and anxiety, on the Brief Symptom Inventory (BSI) scale of the DSFI. FtM transsexuals, however, gave unremarkable responses regarding current symptoms on the BSI (Derogatis et al., 1981). Brown et al. (1996) subsequently used the DFSI to study a large sample of MtF transsexuals, transgenderists, and cross-dressers; for 9 of 10 DFSI subscales, including the BSI, the transgender participants scored within one standard deviation of male norms, and the three transgender groups were not significantly different from each other based on BSI scores.

Studies using other assessment methods likewise have produced conflicting results. Hoenig and Kenna (1974) observed that, based on clinical criteria, about 50% of the MtF and FtM transsexuals they examined displayed significant current psychopathology, including about 12% with either schizophrenia or an affective psychosis. Bodlund and Armelius (1994) diagnosed a current Axis I disorder other than GID in 44% of a small group of MtF and FtM transsexuals, although half of these cases involved only adjustment disorders; in comparison, they found that 82% of patients with a DSM-III-R diagnosis of GIDAANT had another Axis I disorder, with only one third of these being adjustment disorders. De Cuypere et al. (1995) diagnosed a current Axis I disorder other than GID in 23% of their MtF transsexual patients but in none of their FtM transsexual patients. Haraldsen and Dahl (2000) reported that, in a group of MtF and FtM transsexuals undergoing hormone therapy, 33% had a current Axis I disorder. Hepp et al. (2005) diagnosed a current comorbid Axis I disorder in 39% of a small group of patients undergoing

treatment for GID; no significant differences between MtF and FtM patient groups were observed. To put these figures in perspective, the 1-year prevalence among U.S. adults for major Axis I mental disorders, excluding adjustment disorders, is about 26% (Kessler et al., 2005b). Verschoor and Poortinga (1988) found that 21% of MtF transsexuals and 33% of FtM transsexuals reported having received treatment for a psychiatric disorder other than GID at some time in their lives; in the study by De Cuypere et al. (1995), these figures were 45% and 38%, respectively. Hepp et al. (2005) observed a lifetime prevalence of comorbid Axis I disorders in 80% among MtF patients and 54% among FtM patients. In comparison, the lifetime prevalence for major Axis I mental disorders among U.S. adults is about 46% (Kessler et al., 2005a).

Abuse of alcohol and other substances appears to be a problem for many transgender persons, although prevalence estimates vary widely. Cole et al. (1997) documented lifetime histories of substance abuse in 29% of MtF transsexuals and 26% of FtM transsexuals studied. De Cuypere et al. (1995) found even higher lifetime prevalences of substance abuse: 50% in MtF transsexuals and 62% in FtM transsexuals. Verschoor and Poortinga (1988), however, observed much lower substance-abuse prevalences: 11% among MtF transsexuals and only 4% among FtM transsexuals. Clements-Nolle et al. (2001) found that 18% of MtF transgender persons surveyed in San Francisco reported injecting street drugs within the last 6 months. In Philadelphia, Kenagy (2002) observed that 20% of MtF transgender persons but only 6% of FtM transgender persons reported having used injected drugs. In Washington, DC, Xavier (2000) found that 34% of transgender persons believed that they had an alcohol problem, and 36% thought they had a drug problem. Weinberg et al. (1999) surveyed MtF transgender sex workers in San Francisco: 35% used marijuana at least once a week, and 25% used hard drugs at least once a week. For comparison purposes, the 1-year prevalence for substance abuse disorders in U.S. adults is about 9% (Grant et al., 2004b).

Personality disorders are frequently observed in transgender persons. Hoenig and Kenna (1974) diagnosed personality disorders in 18% of their transsexual patients; Haraldsen and Dahl (2000) reported a comparable figure, 20%. Hepp et al. (2005) diagnosed a personality disorder in 42% of their GID patients. The prevalence of personality disorders appears to be higher in persons with nontranssexual types of GID: Bodlund and Armelius (1994) diagnosed a personality disorder in 33% of their transsexual patients but in 73% of their patients with GIDAANT. Similarly, Miach et al. (2000) diagnosed personality disorders in 27% of their transsexual patients but in 65% of their patients with GIDAANT. In comparison, the estimated prevalence of personality disorders in U.S. adults is about 15% (Grant et al., 2004a).

8 Suicide and Self-Harm in Transgender Persons

Transgender persons, and MtF persons especially, appear to be at increased risk for completed suicide, suicide attempts, and other forms of self-harm. In The Netherlands, van Kesteren et al. (1997) reported

that 13 (1.6%) of 816 MtF hormone-treated MtF transsexuals had died of suicide, a percentage more than nine times that of the general population; none of 293 hormone-treated FtM transsexuals had died of suicide. Many transgender persons report having made suicide attempts: Dixen et al. (1984) observed that about 25% of applicants for MtF sex reassignment and 19% of applicants for FtM reassignment gave a history of suicide attempts. Verschoor and Poortinga (1988) found a history of suicide attempts in about 19% of both MtF and FtM transsexuals. Cole et al. (1997) reported that 12% of MtF transsexuals and 21% of FtM transsexuals had attempted suicide. Clements-Nolle et al. (2001) found a lifetime attempted suicide prevalence of 32% in both MtF and FtM transsexuals. De Cuypere et al. (1995) observed still higher lifetime prevalence figures for attempted suicide: 55% in MtF transsexuals and 46% in FtM transsexuals.

Self-mutilation of genitals and breasts is not rare in transgender persons. Dixen et al. (1984) found such a history in 9.4% of applicants for MtF sex reassignment and 2.4% of applicants for FtM reassignment. Cole et al. (1997) observed similar percentages: 8% among MtF transsexuals and 1% among FtM transsexuals. Lothstein (1992) suggested that attempted genital self-mutilation was an underreported symptom of childhood gender dysphoria in boys. Incarcerated transgender persons who are denied access to cross-sex hormones may be at increased risk for this type of self-harm (Meyer et al., 2001). There are multiple case reports of self-castration in MtF transgender persons who are unable to undergo SRS or who anticipate long waiting times for surgery (Krieger et al., 1982; Rana & Johnson, 1993; McGovern, 1995; Murphy et al., 2001; Baltieri & de Andrade, 2005).

9 Violence as a Health Concern in Transgender Persons

Transgender persons appear to be at increased risk for assault, rape, and sexual assault. In a survey of 402 transgender persons, most of whom were cross-dressers or transsexuals, 16% of respondents reported having been a victim of assault within the past year and 3% having been a victim of rape or attempted rape (Lombardi et al., 2001). Respondents' lifetime prevalence of assault was 47% and their lifetime prevalence of rape or attempted rape was 14% (Lombardi et al., 2001). In comparison, in a telephone survey of U.S. adults, only 1.9% of women and 3.4% of men reported having been a victim of assault during the past year, and only 0.3% of women and 0.1% of men reported having been a victim of rape or attempted rape (Tjaden & Thoennes, 2000). Lifetime prevalence of assault among the U.S. adults surveyed was 52% for women and 66% for men, and lifetime prevalence of rape or attempted rape was 18% for women and 3% for men (Tjaden & Thoennes, 2000). Lombardi et al. (2001) found that transgender persons who were younger, who had lower incomes, who were not employed full time, and who identified as transsexual were more likely to report having been a victim of violence at some time in their lives. The prevalence of assault, rape, and attempted rape appears to

be especially high among transgender sex workers. Among a small group of MtF transgender sex workers in Washington, DC, 65% reported having been assaulted since beginning sex work and 35% reported having been raped (Valera et al., 2001).

10 Summary, Conclusions, and Future Perspectives

Some transgender health issues overlap with those of the lesbian, gay, and bisexual (LGB) communities, whereas other transgender health issues are more specialized. The phenomenon that unites the LGB and transgender communities is gender variance. The gender variance of transgender persons is obvious, but LGB persons are also gender-variant in their sexual partner preference and most are gender-variant in other ways as well. Many of the health concerns of LGB communities—especially issues related to mental health, suicide and self-harm, violence, and the sequelae of high-risk sexual behaviors, including HIV infection and other STIs—are plausibly linked to the psychological, social, and economic consequences of living as gender-variant persons in an intolerant society. To the extent that this is true, the health concerns of LGB persons and transgender persons overlap and may find similar solutions. Other transgender health concerns, however, are specific to transgender persons and derive largely from the powerful desire of many transgender persons to change their bodies to more closely reflect their identities. Specific health concerns related to hormone therapy, masculinizing and feminizing surgery, and liquid silicone injection, for example, all reflect transgender persons' often relentless pursuit of bodily transformation.

Cross-sex hormone therapy is highly effective in relieving gender dysphoria and is at least moderately effective in producing physical transformation, especially in FtM transgender persons. Hormone therapy could potentially benefit many more transgender persons than currently receive it, including the many male cross-dressers whose interest in hormones plausibly reflects untreated gender dysphoria. Although potentially the risks of hormone therapy should not be disregarded, reported complications are remarkably infrequent. Postpubertal hormone therapy is, however, limited in the degree of physical transformation it can produce, especially in MtF transgender persons, whose bodies have been irreversibly masculinized by testosterone. The key to increasing the effectiveness of hormone therapy may be earlier intervention, especially increasing the availability of puberty-blocking hormones during the early teenage years. Although earlier hormonal intervention is likely to be controversial in many quarters, initial experience has been encouraging. Transgender health advocates who take issues of prevention seriously should make the initiation of controlled trials of puberty-blocking hormones a high priority.

Transgender persons seek surgery and quasisurgical interventions, such as liquid silicone injections, to try to achieve the physical transformations that hormone therapy alone cannot produce. The quality of transgender surgical procedures is decidedly uneven: MtF SRS is now

highly successful, but there are still no really satisfactory FtM SRS techniques and no satisfactory lower-body tissue augmentation techniques for MtF transgender persons. The deficiencies and complications of FtM SRS and the continued use of liquid silicone injections by MtF transgender persons largely reflect the limitations of current surgical techniques: Although surgeons are very good at removing and rearranging tissue, they are still limited in their ability to augment tissue or to create it de novo. It is likely that FtM SRS will improve incrementally, but developing a truly satisfactory FtM SRS procedure and eliminating the tragic consequences of liquid silicone injections in MtF transgender persons may ultimately depend on advances in biotechnology, especially the development of improved tissue augmentation materials and effective techniques for in vitro tissue and organ culture. Given these difficult realities, the specialized health concerns of transgender persons are likely to continue to challenge clinicians and researchers for the foreseeable future.

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